

Please amend the application as follows:

IN THE SPECIFICATION

On page 12, line 7, after the amino acid sequence ending in "CysArgThrGlyAspArg" please insert -- (SEQ ID NO:121) --.

On page 13, line 23, "glycosylation" is misspelled. Please delete the second "n" at the end of "glycosylation".

On page 24, line 19, after the amino acid sequence Gly-Gly-Gly-Ser, please insert -- (SEQ ID NO:123) -- .

On page 25, line 20, after the amino acid sequence Gly-Gly-Gly-Ser, please insert -- (SEQ ID NO:123) -- .

Please replace the sequence listing on pages 45-92 with the Substitute Sequence listing (pages numbered S1-S59) submitted herewith.

Please replace Figure 5 with the substitute Figure 5, submitted herewith, in which the sequence listing identifiers have been indicated.

IN THE CLAIMS

Please amend the claims as follows:

Please amend claim 1 as follows:

1. (once amended) A human Erythropoietin [EPO] receptor agonist polypeptide, comprising a modified Erythropoietin [EPO] amino acid sequence [of the Formula] selected from the group consisting of:

(a) the sequence of SEQ ID NO:121;

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[AlaProProArgLeuIleCysAspSerArgValLeuGluArgTyrLeuLeuGluAlaLys
10 20

GluAlaGluAsnIleThrThrGlyCysAlaGluHisCysSerLeuAsnGluAsnIleThr
30 40

ValProAspThrLysValAsnPheTyrAlaTrpLysArgMetGluValGlyGlnGlnAla
50 60

ValGluValTrpGlnGlyLeuAlaLeuLeuSerGluAlaValLeuArgGlyGlnAlaLeu
70 80

LeuValAsnSerSerGlnProTrpGluProLeuGlnLeuHisValAspLysAlaValSer
90 100

GlyLeuArgSerLeuThrThrLeuLeuArgAlaLeuGlyAlaGlnLysGluAlaIleSer
110 120

ProProAspAlaAlaSerAlaAlaProLeuArgThrIleThrAlaAspThrPheArgLys
130 140

LeuPheArgValTyrSerAsnPheLeuArgGlyLysLeuLysLeuTyrThrGlyGluAla
150 160

CysArgThrGlyAspArg SEQ ID NO:121

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(b) a polypeptide sequence comprising residues 7-
166 of SEQ ID NO:121;

(c) a polypeptide sequence comprising residues 1-
161 of SEQ ID NO:121; and

(d) a polypeptide sequence comprising residues 7-
161 of SEQ ID NO:121;

and wherein said modification comprises the linear
rearrangement of the sequences of (a)-(d) wherein the N-
terminus is joined to the C-terminus directly or through a
linker capable of joining the N-terminus to the C-terminus
and [having] new C- and N-termini [at amino acids] are
created between the amino acid residue pairs of SEQ ID NO:1
selected from the group consisting of:

23-24, 24-25, 25-26, 26-27, 27-28, 28-29, 29-30, 30-31, 31-
32, 32-33, 33-34, 34-35, 35-36, 36-37, 37-38, 38-39, 40-41,
41-42, 43-44, 44-45, 45-46, 46-47, 47-48, 48-49, 50-51, 51-
52, 52-53, 53-54, 54-55, 55-56, 56-57, 57-58, 77-78, 78-79,
79-80, 80-81, 81-82, 82-83, 84-85, 95-86, 86-87, 87-88, 88-
89, 108-109, 109-110, 110-111, 111-112, 112-113, 113-114,
114-115, 115-116, 116-117, 117-118, 118-119, 119-120, 120-
121, 121-122, 122-123, 123-124, 124-125, 125-126, 126-127,
127-128, 128-129, 129-130, 130-131, 131-132; [respectively]
and

~~wherein said **Erythropoietin [EPO]** receptor agonist polypeptide may optionally be immediately preceded by (methionine⁻¹), (alanine⁻¹) or (methionine⁻², alanine⁻¹).~~

2. (once amended) The **Erythropoietin [EPO]** receptor agonist polypeptide, as recited in claim 1, wherein said linker is selected from the group consisting of;

GlyGlyGlySer SEQ ID NO:123;

GlyGlyGlySerGlyGlyGlySer SEQ ID NO:124;

GlyGlyGlySerGlyGlyGlySerGlyGlySer SEQ ID NO:125;

SerGlyGlySerGlyGlySer SEQ ID NO:126;

GluPheGlyAsnMet SEQ ID NO:127;

GluPheGlyGlyAsnMet SEQ ID NO:128;

GluPheGlyGlyAsnGlyGlyAsnMet SEQ ID NO:129; and

GlyGlySerAspMetAlaGly SEQ ID NO:130.

3. (once amended) The **Erythropoietin [EPO]** receptor agonist polypeptide of claim 1 selected from the group consisting of;

SEQ ID NO:1; SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:13; SEQ ID NO:14; SEQ ID NO:15; SEQ ID NO:16; SEQ ID NO:17; SEQ ID NO:18; SEQ ID NO:19; SEQ ID NO:20; SEQ ID NO:21; SEQ ID NO:22; SEQ ID NO:23; SEQ ID NO:24; SEQ ID NO:25; SEQ ID NO:26; SEQ ID NO:27; SEQ ID NO:28; SEQ ID NO:29; SEQ ID NO:30; SEQ ID NO:31; SEQ ID NO:32; SEQ ID NO:33; SEQ ID NO:34; SEQ ID NO:35; SEQ ID NO:36; SEQ ID NO:37; SEQ ID NO:38; SEQ ID NO:39; SEQ ID NO:40; SEQ ID NO:41; SEQ ID NO:42; SEQ ID NO:43; SEQ ID NO:44; SEQ ID NO:45; SEQ ID

NO:46; SEQ ID NO:47; SEQ ID NO:48; SEQ ID NO:49; SEQ ID NO:50; SEQ ID NO:51; SEQ ID NO:52; SEQ ID NO:53; SEQ ID NO:54; SEQ ID NO:55; SEQ ID NO:56; SEQ ID NO:57; SEQ ID NO:58; SEQ ID NO:59 and SEQ ID NO:122.

4. (once amended) The Erythropoietin [EPO] receptor agonist polypeptide of claim 3 wherein the [linker] polypeptide sequence ([Gly]GlyGlyGlySer SEQ ID NO:123) in SEQ ID NO:1; SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:13; SEQ ID NO:14; SEQ ID NO:15; SEQ ID NO:16; SEQ ID NO:17; SEQ ID NO:18; SEQ ID NO:19; SEQ ID NO:20; SEQ ID NO:21; SEQ ID NO:22; SEQ ID NO:23; SEQ ID NO:24; SEQ ID NO:25; SEQ ID NO:26; SEQ ID NO:27; SEQ ID NO:28; SEQ ID NO:29; SEQ ID NO:30; SEQ ID NO:31; SEQ ID NO:32; SEQ ID NO:33; SEQ ID NO:34; SEQ ID NO:35; SEQ ID NO:36; SEQ ID NO:37; SEQ ID NO:38; SEQ ID NO:39; SEQ ID NO:40; SEQ ID NO:41; SEQ ID NO:42; SEQ ID NO:43; SEQ ID NO:44; SEQ ID NO:45; SEQ ID NO:46; SEQ ID NO:47; SEQ ID NO:48; SEQ ID NO:49; SEQ ID NO:50; SEQ ID NO:51; SEQ ID NO:52; SEQ ID NO:53; SEQ ID NO:54; SEQ ID NO:55; SEQ ID NO:56; SEQ ID NO:57; SEQ ID NO:58; SEQ ID NO:59 and SEQ ID NO:122 is a [linker] polypeptide sequence selected from the group consisting of;

GlyGlyGlySerGlyGlySer SEQ ID NO:124;

GlyGlyGlySerGlyGlySerGlyGlySer SEQ ID NO:125;

SerGlyGlySerGlyGlySer SEQ ID NO:126;

GluPheGlyAsnMet SEQ ID NO:127;

GluPheGlyGlyAsnMet SEQ ID NO:128;

GluPheGlyGlyAsnGlyGlyAsnMet SEQ ID NO:129; and
GlyGlySerAspMetAlaGly SEQ ID NO:130.

5. (once amended) A nucleic acid molecule comprising a DNA sequence encoding the Erythropoietin [EPO] receptor agonist polypeptide of claim 1.

6. (once amended) A nucleic acid molecule comprising a DNA sequence encoding the Erythropoietin [EPO] receptor agonist polypeptide of claim 2.

7. (once amended) A nucleic acid molecule comprising a DNA sequence encoding the Erythropoietin [EPO] receptor agonist polypeptide of claim 3.

8. (once amended) A nucleic acid molecule comprising a DNA sequence encoding the Erythropoietin [EPO] receptor agonist polypeptide of claim 3 selected from the group consisting of;

SEQ ID NO:60; SEQ ID NO:61; SEQ ID NO:62; SEQ ID NO:63; SEQ ID NO:64; SEQ ID NO:65; SEQ ID NO:66; SEQ ID NO:67; SEQ ID NO:68; SEQ ID NO:69; SEQ ID NO:70; SEQ ID NO:71; SEQ ID NO:72; SEQ ID NO:73; SEQ ID NO:74; SEQ ID NO:75; SEQ ID NO:76; SEQ ID NO:77; SEQ ID NO:78; SEQ ID NO:79; SEQ ID NO:80; SEQ ID NO:81; SEQ ID NO:82; SEQ ID NO:83; SEQ ID NO:84; SEQ ID NO:85; SEQ ID NO:86; SEQ ID NO:87; SEQ ID NO:88; SEQ ID NO:89; SEQ ID NO:90; SEQ ID NO:91; SEQ ID NO:92; SEQ ID NO:93; SEQ ID NO:94; SEQ ID NO:95; SEQ ID NO:96; SEQ ID NO:97; SEQ ID NO:98; SEQ ID NO:99; SEQ ID NO:100; SEQ ID NO:101; SEQ ID NO:102; SEQ ID NO:103; SEQ ID NO:104; SEQ ID NO:105; SEQ ID NO:106; SEQ ID NO:107; SEQ ID

NO:108; SEQ ID NO:109; SEQ ID NO:110; SEQ ID NO:111; SEQ ID NO:112; SEQ ID NO:113; SEQ ID NO:114; SEQ ID NO:115; SEQ ID NO:116; SEQ ID NO:117; SEQ ID NO:118 and SEQ ID NO:119.

9. (once amended) A nucleic acid molecule comprising a DNA sequence encoding the Erythropoietin [EPO] receptor agonist polypeptide of claim 4.

10. (once amended) A method of producing a Erythropoietin [EPO] receptor agonist polypeptide comprising: growing under suitable nutrient conditions, a host cell transformed or transfected with a replicable vector comprising said nucleic acid molecule of claim 5, 6, 7, 8 or 9 in a manner allowing expression of said Erythropoietin [EPO] receptor agonist polypeptide and recovering said Erythropoietin [EPO] receptor agonist polypeptide.

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11. (once amended) A composition comprising; a Erythropoietin [EPO] receptor agonist polypeptide according to claim 1, 2, 3 or 4; and a pharmaceutically acceptable carrier.

12. (once amended) A composition comprising; a Erythropoietin [EPO] receptor agonist polypeptide according to claim 1, 2, 3 or 4; a second protein [factor]; and a pharmaceutically acceptable carrier.

13. (once amended) The composition of claim 12 wherein said second protein [factor] is selected from the group consisting of: GM-CSF, G-CSF, c-mpl ligand, M-CSF, IL-1, IL-

4, IL-2, IL-3, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, LIF, flt3/flk2 ligand, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor, and stem cell factor, IL-3 variant[s], fusion protein[s], G-CSF receptor agonist[s], c-mpl receptor agonist[s], IL-3 receptor agonist[s], and multi-functional receptor agonist[s].

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14. (once amended) A method of stimulating the production of hematopoietic cells in a patient comprising the step of; administering a Erythropoietin [EPO] receptor agonist polypeptide of claim 1, 2, 3 or 4, to said patient [patent].

REMARKS

Election/Restriction

Applicants acknowledge that the restriction is maintained and is made FINAL and claims 15-22 have been withdrawn from consideration by the Examiner as drawn to a non-elected invention. Applicants reserve the right to continue prosecution of non-elected claims 15-22 (Groups II & III) in one or more continuing applications.

Sequence Rules

The Examiner objected to the application as not being fully compliant with the sequence rules under 37 C.F.R. § 1.821-1.825, because each disclosure of a sequence is not